UN 30 ::

SEQUENCE LISTING

02

10> WALLACH, David
GOLTSEV, Yura
KOVALENKO, Andrei
VARFOLOMEEV, Eugene
BRODIANSKI, Vadim



<120> ASH (CASPASE HOMOLOGUE) WITH DEATH EFFECTOR DOMAIN, MODULATORS OF THE FUNCTION OF FAS RECEPTORS

<130> WALLACH=23

<140> 09/380****546

<141> 1999-11-29

<150> PCT/IL98/0098

<151> 1998-02-26

<150> IL 120367

<151> 1997-03-03

<150> IL120759

<151> 1997-05-01

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Lys Leu Ser Val Gly Asp Leu Ala Glu Leu Leu Tyr Arg Val Arg Arg
Phe Asp Leu Lys Arg Ile Leu Lys Met Asp Arg Lys Ala Val Glu
Thr His Leu Leu Asn Pro His Leu Val Ser Asp Tyr Arg Val Leu Met
Ala Glu Ile Gly Glu Asp Leu Asp Lys Ser Asp Val Ser Ser Leu Ile
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Lys Leu Ser Val Gly Asp Leu Ala Glu Leu Leu Tyr Arg Val Arg Arg
Phe Asp Leu Leu Lys Arg Ile Leu Lys Met Asp Arg Lys Ala Val Glu
Thr His Leu Leu Arg Asn Pro His Leu Val Ser Asp Tyr Arg Val Leu
Met Ala Glu Ile Gly Glu Asp Leu Asp Lys Ser Asp Val Ser Ser Leu
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Arg Ile Asp Leu Lys Thr Lys Ile Gln Lys Tyr Lys Gln Ser Val Gln 165 170 175

Gly Ala Gly Thr Ser Tyr Arg Asn Val Leu Gln Ala Ala Ile Gln Lys 180 185 190

Ser Leu Lys Asp Pro Ser Asn Asn Phe Arg Met Ile Thr Pro Tyr Ala 195 200 205

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Leu Ser Glu Arg Gly Gln Leu Ser Phe Ala Thr Leu Ala Glu Leu Leu 50 55 60

Tyr Arg Val Arg Arg Phe Asp Leu Leu Lys Arg Ile Leu Lys Thr Asp 65 70 75 80

Lys Ala Thr Val Glu Asp His Leu Arg Arg Asn Pro His Leu Val Ser 85 90 95

Asp Tyr Arg Val Leu Leu Met Glu Ile Gly Glu Ser Leu Asp Gln Asn 100 105 110

Asp Val Ser Ser Leu Val Phe Leu Thr Arg Ile Thr Arg Asp Tyr Thr 115 120 125

Gly Arg Gly Lys Ile Ala Lys Asp Lys Ser Phe Leu Asp Leu Val Ile 130 135 140

Glu Leu Glu Lys Leu Asn Leu Ile Ala Ser Asp Gln Leu Asn Leu Leu 145 150 155 160

Glu Lys Cys Leu Lys Asn Ile His Arg Ile Asp Leu Asn Thr Lys Ile 170 Gln Lys Tyr Thr Gln Ser Ser Gln Gly Ala Arg Ser Asn Met Asn Thr Leu Gln Ala Ser Leu Pro Lys Leu Ser Ile Lys Tyr Asn Ser Arg Leu Gln Asn Gly Arg Ser Lys Glu Pro Arg Phe Val Glu Tyr Arg Asp Ser Gln Arg Thr Leu Val Lys Thr Ser Ile Gln Glu Ser Gly Ala Phe Leu 230 235 Pro Pro His Ile Arg Glu Glu Thr Tyr Arg Met Gln Ser Lys Pro Leu Gly Ile Cys Leu Ile Ile Asp Cys Ile Gly Asn Asp Thr Lys Tyr Leu 265 Gln Glu Thr Phe Thr Ser Leu Gly Tyr His Ile Gln Leu Phe Leu Phe Pro Lys Ser His Asp Ile Thr Gln Ile Val Arg Arg Tyr Ala Ser Met 295 Ala Gln His Gln Asp Tyr Asp Ser Phe Ala Cys Val Leu Val Ser Leu Gly Gly Ser Gln Ser Met Met Gly Arg Asp Gln Val His Ser Gly Phe 330 Ser Leu Asp His Val Lys Asn Met Phe Thr Gly Asp Thr Cys Pro Ser Leu Arg Gly Lys Pro Lys Leu Phe Phe Ile Gln Asn Tyr Glu Ser Leu Gly Ser Gln Leu Glu Asp Ser Ser Leu Glu Val Asp Gly Pro Ser Ile Lys Asn Val Asp Ser Lys Pro Leu Gln Pro Arg His Cys Thr Thr His Pro Glu Ala Asp Ile Phe Trp Ser Leu Cys Thr Ala Asp Val Ser His 405 Leu Glu Lys Pro Ser Ser Ser Ser Val Tyr Leu Gln Lys Leu Ser 425 Gln Gln Leu Lys Gln Gly Arg Arg Pro Leu Val Asp Leu His Val 435 Glu Leu Met Asp Lys Val Tyr Ala Trp Asn Ser Gly Val Ser Ser Lys

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Val Pro Pro Asn Val Arg Asp Leu Leu Asp Ile Leu Arg Glu Arg Gly 35 40 45

Lys Leu Ser Val Gly Asp Leu Ala Glu Leu Leu Tyr Arg Val Arg Arg 50 55 60

Phe Asp Leu Leu Lys Arg Ile Leu Lys Met Asp Arg Lys Ala Val Glu 65 70 75 80

Thr His Leu Leu Arg Asn Pro His Leu Val Ser Asp Tyr Arg Val Leu 85 90 95

Met Ala Glu Ile Gly Glu Asp Leu Asp Lys Ser Asp Val Ser Ser Leu 100 105 110

Ile Phe Leu Met Lys Asp Tyr Met Gly Arg Gly Lys Ile Ser Lys Glu 115 120 125

Lys Ser Phe Leu Asp Leu Val Val Glu Leu Glu Lys Leu Asn Leu Val 130 135 . 140

Ala Pro Asp Gln Leu Asp Leu Leu Glu Lys Cys Leu Lys Asn Ile His 145 150 155 160

Arg Ile Asp Leu Lys Thr Lys Ile Gln Lys Tyr Lys Gln Ser Val Gln 165 170 175

Gly Ala Gly Thr Ser Tyr Arg Asn Val Leu Gln Ala Ala Ile Gln Lys 180 185 190

Ser Leu Lys Asp Pro Ser Asn Asn Phe Arg Met Ile Thr Pro Tyr Ala 195 200 205

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Glu Lys Glu Met Leu Leu Phe Leu Cys Arg Asp Val Ala Ile Asp Val 20 25 30

Val Pro Pro Asn Val Arg Asp Leu Leu Asp Ile Leu Arg Glu Arg Gly 35 40 45

Lys Leu Ser Val Gly Asp Leu Ala Glu Leu Leu Tyr Arg Val Arg Arg 50 55 60

Phe Asp Leu Leu Lys Arg Ile Leu Lys Met Asp Arg Lys Ala Val Glu 65 70 75 80

Thr His Leu Leu Arg Asn Pro His Leu Val Ser Asp Tyr Arg Val Leu 85 90 95

Met Ala Glu Ile Gly Glu Asp Leu Asp Lys Ser Asp Val Ser Ser Leu 100 105 110

Ile Phe Leu Met Lys Asp Tyr Met Gly Arg Gly Lys Ile Ser Lys Glu , \$115\$ \$120\$ \$125\$

Lys Ser Phe Leu Asp Leu Val Val Glu Leu Glu Lys Leu Asn Leu Val 130 135 140

Ala Pro Asp Gln Leu Asp Leu Leu Glu Lys Cys Leu Lys Asn Ile His 145 150 155 160

Arg Ile Asp Leu Lys Thr Lys Ile Gln Lys Tyr Lys Gln Ser Val Gln 165 170 175

Gly Ala Gly Thr Ser Tyr Arg Asn Val Leu Gln Ala Ala Ile Gln Lys 180 185 190

Ser Leu Lys Asp Pro Ser Asn Asn Phe Arg Leu His Asn Gly Arg Ser 195 200 205

Lys Glu Gln Arg Leu Lys Glu Gln Leu Gly Ala Gln Gln Glu Pro Val 210 215 220

Lys Lys Ser Ile Gln Glu Ser Glu Ala Phe Leu Pro Gln Ser Ile Pro 225 230 235 240

Glu Glu Arg Tyr Lys Met Lys Ser Lys Pro Leu Gly Ile Cys Leu Ile 245 250 255

Ile Asp Cys Ile Gly Asn Glu Thr Glu Leu Leu Arg Asp Thr Phe Thr 260 265 270

Ser Leu Gly Tyr Glu Val Gln Lys Phe Leu His Leu Ser Met His Gly 275 280 285

Ile Ser Gln Ile Leu Gly Gln Phe Ala Cys Met Pro Glu His Arg Asp 290 295 300

Tyr Asp Ser Phe Val Cys Val Leu Val Ser Arg Gly Gly Ser Gln Ser 305 310 315 320

Val Tyr Gly Val Asp Gln Thr His Ser Gly Leu Pro Leu His His Ile 325 330 335

Arg Arg Met Phe Met Gly Asp Ser Cys Pro Tyr Leu Ala Gly Lys Pro $340 \hspace{1cm} 345 \hspace{1cm} 350$

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Asn Ser Ser Leu Leu Glu Val Asp Gly Pro Ala Met Lys Asn Val Glu 370 375 380

Phe Lys Ala Gln Lys Arg Gly Leu Cys Thr Val His Arg Glu Ala Asp 385 390 395 400

Phe Phe Trp Ser Leu Cys Thr Ala Asp Met Ser Leu Leu Glu Gln Ser 405 410 415

His Ser Ser Pro Ser Leu Tyr Leu Gln Cys Leu Ser Gln Lys Leu Arg 420 425 430

Gln Glu Arg Lys Arg Pro Leu Leu Asp Leu His Ile Glu Leu Asn Gly 435 440 445

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35 40 45

Gln Glu Lys Arg Met Leu Glu Glu Ser Asn Leu Ser Phe Leu Lys Glu 50 55 60

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Leu Gly Met Ala Thr Val Asn Asn Cys Val Ser Tyr Arg Asn Pro Ala 405 410 415

Glu Gly Thr Trp Tyr Ile Gln Ser Leu Cys Gln Ser Leu Arg Glu Arg 420 425 430

Cys Pro Arg Gly Asp Asp Ile Leu Thr Ile Leu Thr Glu Val Asn Tyr 435 440 45

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Val Gln Asp Val Glu Asn Leu Lys Phe Leu Cys Ile Gly Leu Val Pro 35 40 45

Asn Lys Lys Leu Glu Lys Ser Ser Ser Ala Ser Asp Val Phe Glu His 50 55 60

Leu Leu Ala Gly Asp Leu Leu Ser Glu Glu Asp Pro Phe Phe Leu Ala 65 70 75 80

Glu Leu Leu Tyr Ile Ile Arg Gln Lys Lys Leu Leu Gln His Leu Asn 85 90 95

Cys Thr Lys Glu Glu Val Glu Arg Leu Leu Pro Thr Arg Gln Arg Val 100 105 110

Ser Leu Phe Arg Asn Leu Leu Tyr Glu Leu Ser Glu Gly Ile Asp Ser 115 120 125

Glu Asn Leu Lys Asp Met Ile Phe Leu Leu Lys Asp Ser Leu Pro Lys 130 135 140

Thr Glu Met Thr Ser Leu Ser Phe Leu Ala Phe Leu Glu Lys Gln Gly 145 150 155 160

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Thr Phe Arg Asn Leu Lys Tyr Glu Val Arg Asn Lys Asn Asp Leu Thr

Arg Glu Glu Ile Val Glu Leu Met Arg Asp Val Ser Lys Glu Asp His

Ser Lys Arg Ser Ser Phe Val Cys Val Leu Leu Ser His Gly Glu Glu

Gly Ile Ile Phe Gly Thr Asn Gly Pro Val Asp Leu Lys Lys Ile Thr 105

Asn Phe Phe Arg Gly Asp Arg Cys Arg Ser Leu Thr Gly Lys Pro Lys

Leu Phe Ile Ile Gln Ala Cys Arg Gly Thr Glu Leu Asp Cys Gly Ile

Glu Thr Asp Ser Gly Val Asp Asp Asp Met Ala Cys His Lys Ile Pro 145

Val Glu Ala Asp Phe Leu Tyr Ala Tyr Ser Thr Ala Pro Gly Tyr Tyr

Ser Trp Arg Asn Ser Lys Asp Gly Ser Trp Phe Ile Gln Ser Leu Cys

Ala Met Leu Lys Gln Tyr Ala Asp Lys Leu Glu Phe Met His Ile Leu

Thr Arg Val Asn Arg Lys Val Ala Thr Glu Phe Glu Ser Phe Ser Phe 215 210

Asp Ala Thr Phe His Ala Lys Lys Gln Ile Pro Cys Ile Val Ser Met 235 230

Leu Thr Lys Glu Leu Tyr Phe Tyr His

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Ser Leu Glu Glu Ala Gln Arg Ile Trp Lys Gln Lys Ser Ala Glu Ile 35 40 45

Tyr Pro Ile Met Asp Lys Ser Ser Arg Thr Arg Leu Ala Leu Ile Ile
50 55 60

Cys Asn Glu Glu Phe Asp Ser Ile Pro Arg Arg Thr Gly Ala Glu Val 65 70 75 80

Asp Ile Thr Gly Met Thr Met Leu Leu Gln Asn Leu Gly Tyr Ser Val 85 90 95

Asp Val Lys Lys Asn Leu Thr Ala Ser Asp Met Thr Thr Glu Leu Glu 100 105 110

Ala Phe Ala His Arg Pro Glu His Lys Thr Ser Asp Ser Thr Phe Leu 115 120 125

Val Phe Met Ser His Gly Ile Arg Glu Gly Ile Cys Gly Lys Lys His 130 135 140

Ser Glu Gln Val Pro Asp Ile Leu Gln Leu Asn Ala Ile Phe Asn Met 145 150 155 160

Leu Asn Thr Lys Asn Cys Pro Ser Leu Lys Asp Lys Pro Lys Val Ile 165 170 175

Ile Ile Gln Ala Cys Arg Gly Asp Ser Pro Gly Val Val Trp Phe Lys 180 185 190

Asp Ser Val Gly Val Ser Gly Asn Leu Ser Leu Pro Thr Thr Glu Glu 195 200 205

Phe Glu Asp Asp Ala Ile Lys Lys Ala His Ile Glu Lys Asp Phe Ile 210 215 220

Ala Phe Cys Ser Ser Thr Pro Asp Asn Val Ser Trp Arg His Pro Thr 225 230 235 240

Met Gly Ser Val Phe Ile Gly Arg Leu Ile Glu His Met Gln Glu Tyr
245 250 255

Ala Cys Ser Cys Asp Val Glu Glu Ile Phe Arg Lys Val Arg Phe Ser 260 265 270

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